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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/880,702	06/13/2001	Katherine A. High	0800-0024	5537

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 08/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/880,702	HIGH, KATHERINE A.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6,7,13,14,16,17,18,19,20,27,28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6,7,13,14,16-20,27,28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Final Rejection

Claims 1, 2, 6, 7, 13, 14, 16-20, and 27-28 are pending.

Applicant's traversal, the amendment to claims 1 and 13, and the addition of claims 27 and 28 in paper filed on is acknowledged and considered.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application 60/211,066 upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 1, 2, 6, 7, 13, 14, 16-20 and 27-28 of this application.

Instant claims 1, 2, 6, 7, 13, 14, 16-20, and 27-28: the provisional 60/211,066 does not provide sufficient written description for a method of delivering rAAV virions to the bile duct or to the ducts of the submandibular gland because the provisional does not recite a method of delivering rAAV virions to the bile duct or to the ducts of the submandibular gland.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of gene therapy comprising delivering a

recombinant adeno-associated virus (rAAV) virions comprising a heterologous gene encoding a Factor IX protein to the bile duct system or to the ducts of the submandibular gland of a human, does not reasonably provide enablement for a method of gene therapy in a mammal comprising delivering rAAV virions comprising a heterologous gene encoding any other protein to the bile duct system or to the ducts of the submandibular gland of said human. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The invention is directed to a gene therapy method in a human comprising delivering rAAV virions to the bile duct system or to the ducts of the submandibular gland of said human. The invention embraces treating any disease or disorder in a human using the claimed gene therapy method. The field of the invention lies in gene therapy.

Furthermore, and with respect to claims directed to any gene therapy directed to any treatment of a human; the state of the art exemplified by Anderson et al., *Nature*, Vol. 392, pp. 25-30, 1998, displays major consideration for any gene transfer or any DNA therapy protocol involve issues that include:

1) The type of vector and amount of DNA constructs to be administered,

2) The route and time course of administration, the sites of administration, and successful uptake of the claimed DNA at the target site;

3) The trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA product, the amount and stability of the protein produced, and

4) What amount of the expressed proteins considered to be therapeutically effective for a DNA therapy method.

In addition, all of these issues differ dramatically based on the specific vector used, the route of administration, the animal being treated, therapeutically effective amount of the DNA, and the disease being treated.

Anderson teaches that gene therapy is a powerful new technology that still requires several years before it will make a noticeable impact on the treatment of disease, and that several major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered (pp. 25-30).

Anderson further teaches that the reason for the low efficiency of gene transfer and expression in human patients is that we still lack the basis understanding of how vectors should be constructed what regulatory sequences are appropriated for which cell types (page 30, column 1, last paragraph). Furthermore, Verma, *Nature*, Vol. 389, pages 239-242, 1997, indicates that factors including the nature of the diseases and/or disorders, the nature of a DNA and/or target tissue, and a delivery system and/or amounts of the DNA complexes employed in the delivery system that would generate a therapeutic effect *in vivo* must be considered for any gene therapy method to be successful (page 238, columns 1 and 2). Therefore, at the time the application was filed, gene therapy was considered unpredictable.

The applicant teaches administering rAAV virions comprising a heterologous nucleic acid encoding Factor IX to the anterior thigh in adult hemophiliac patients and studying the location of rAAV virions and expression of Factor IX in different tissues of the patients (pages 16-22). Applicant contemplates delivering rAAV virions to the hepatic artery of humans or directly to the liver of a human with pre-existing antibodies (pages 23-24).

The specification provides sufficient guidance and/or factual evidence for treating hemophilia in a human using rAAV virion comprising a heterologous gene encoding a Factor IX protein operably linked to expression control elements. However, in view of the In Re Wands Factors, the as-filed specification does not provide sufficient guidance and/or factual evidence for one skilled in the art to use the full scope of the claimed invention. The breadth of the claimed methods embraces treating a variety of diseases or disorders (see pages 10-12) in a human using the claimed gene therapy method that are not taught by the prior art or the as-filed specification.

The prior art teaches several problems with gene therapy (See Rubanyi, Molecular Aspects of Medicine, Vol. 22, 2001, pages 113-142; Anderson, *supra*; and Verma, *supra*).

In addition, the breath of the claims embrace treating a disease or a disorder in a human using the claimed method and each method would require a certain amount of gene expression in a particular organ or tissue of the human to observe a therapeutic effect. For example, some lysosomal disorders result from lack of expression of an enzyme in several tissues including the brain (e.g., Fabry disease). The applicant does not teach one skilled in the art how a therapeutic effect in the brain of a human with the lysosomal disorder results from expressing the gene product in a secretory gland (e.g., duct of a liver) of the human. In addition, the specification

does not teach one skilled in the art how to use the claimed method to circumvent the blood/brain barrier to express a protein at a therapeutic level in the brain of a human. Furthermore, as taught in the art of record, gene therapy requires more than just providing a human with a rAAV virion comprising a heterologous gene encoding a therapeutic protein. For example, gene therapy for type 1-diabetes is the development of beta-cell substitutes by introducing an insulin-producing gene into non-beta cells, which would evade the beta-cell-specific autoimmune attack. However, this therapy has been hampered by the absence of (1) an appropriate glucose-sensing system to regulate insulin gene transcription; (2) enzymes that process proinsulin to insulin; and (3) glucose-regulatable exocytosis in the target cells. The applicant does not provide sufficient guidance and/or factual evidence for using the claimed method to treat a human with type-1 diabetes. The specification does not provide sufficient guidance and/or factual evidence for one skilled in the art to practice a genus of delivering a heterologous gene to the bile duct system or to the ducts of the submandibular gland of a human and therapeutically expressing the heterologous gene product in any tissue or organ to treat a genus of diseases or disorders in said human. Applicant and the prior art teach the using rAAV virions comprising a heterologous nucleic acid encoding Factor IX to treat hemophilia in a human. However, the relevance of this data to treatment of a genus of diseases and/or disorders is unclear at best because neither the applicant nor the prior art provide a correlation or nexus between the results obtained in hemophiliac patients such as those provide by applicant with results which the skilled artisan would reasonably expect to see for a genus of diseases or disorders using the claimed method. Thus, in view of the In Re Wands Factors, the as-filed specification does not provide sufficient guidance for how to reasonably extrapolate from to a genus of treating a disease or disorder by

contacting the bile duct system or to the ducts of the submandibular gland of a human to provide a therapeutic effect in any tissue or organ for a disease or disorder.

In addition, with respect to using rAAV virion to treat a genus of diseases or disorders in a human contemplated by the specification, it is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of an invention in order to constitute adequate enablement, e.g. Genentech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366, 42, USPQ2d 1001, 1005 (Fed. Cir. 1997).

Furthermore, the court in Enzo 188 F.3d at 1374, 52 USPQ2d at 1138 states:

> It is well settled that patent applications are not required to disclose every species encompassed by their claims, even in an unpredictable art. However, there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. In re Vaeck, 947 F.2d 48, 496 & n.23. 30 USPQ2d 1438, 1445 &n23 (Fed. Cir. 1991)(citation omitted). Here, however, the teachings set forth in the specification provide no more than a "plan" or "invitation" for those of skill in the art to experiment...; they do not provide sufficient guidance or specificity as to how to execute that plan. See Fiers v. Revel. 984 F.2d.1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993); In re Wright, 999 F.2d...[1557], 1562, 27 USPQ2d...[1510], 1514. [Footnote omitted].

On this record, it is apparent that the specification provides no more than a plan or invitation in view of the art of record exemplifying the unpredictability of gene therapy, for those skilled in the art to experiment with the level of heterologous gene expression so as to provide a therapeutic effect as intended by the as-filed specification at the time the invention was made. See also Genentech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366, 42, USPQ2d 1001, 1005 (Fed. Cir. 1997)

> ("Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable the public to understand and carry out the invention.")

In view of the art of record and the lack of guidance provided by the specification for treating any disease and/or disorder other than hemophilia using the claimed method; the specification does not provide reasonable detail for what protocols are required for each different method of

gene therapy embraced by the claims, and it would take one skilled in the art an undue amount of experimentation to reasonably extrapolate from the specification to the full breadth of the claimed invention. Therefore, the as-filed specification is not enabled for the full scope of the claimed methods.

In addition, the art of record teaches problems with using rAAV in gene therapy. See Hortelano et al., (Art. Cells, Blood Subs., and Immod. Biotech 28:1-24, 2000) and Wang et al., (PNAS, Vol. 97, pages 13714-13719, 2000). The genome of AAV is only 4.7kb-5.0kb, which is too short to use for delivering some nucleic acid sequences, e.g., full-size of hFVIII cDNA, CFTR, and the dystrophin gene. Hortelano teaches, "Despite the promising results obtained with AAV vectors delivering FIX, it has not yet been used to deliver FVIII (page 10)." Wang teaches, "AAV are too small (5kb) to package the 14-kb dystrophin cDNA (page 13714)." The specification does not teach one skilled in the art how to overcome the size limitation of AAV vectors. The applicant's disclosure does not provide sufficient guidance and/or factual evidence for the art at the time the invention was filed used to overcome the problems associated with AAV size limitation.

In view of the In Re Wands Factors, it would take one skilled in the art an undue amount of experimentation to practice the full breadth of the claimed invention. As a result, it is not apparent how one skilled in the art determines, without undue experimentation, which of the claimed rAAV virion generates a therapeutic effect, how is it apparent as to how one skilled in the art, without any undue experimentation, practices any gene therapy method as contemplated by the claims, particularly given the unpredictability of gene therapy as a whole and/or the doubts expressed in the art of record.

In conclusion, the as-filed specification and claims coupled with the prior art at the time the invention was made only provide sufficient guidance and/or evidence to reasonably enable the for a method of gene therapy comprising delivering a recombinant adeno-associated virus (rAAV) virions comprising a heterologous gene encoding a Factor IX protein to the bile duct system or to the ducts of the submandibular gland of a human and not for the full breadth of the claimed methods. Given that gene therapy wherein any rAAV is employed to correct a disease or a medical condition in any human was unpredictable at the time the invention was made, and given the lack of sufficient guidance as to a gene therapy effect produced by any rAAV virion cited in the claims, one skilled in the art would have to engage in a large quantity of experimentation in order to practice the claimed invention based on the applicant's disclosure and the unpredictability of gene therapy.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (f) he did not himself invent the subject matter sought to be patented.

Claims 27 and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by Wolff et al., (US 2001/0009904) as evident by Couto et al. (US Patent 6,200,560).

Wolff teaches delivering AAV comprising a heterologous nucleic acid to the bile duct of a human, wherein the heterologous nucleic acid is expressed at a therapeutic level (pages 1, 2, 4, and 16).

Couto teaches that 85% of the human population is seropositive for AAV-2 serotype (column 12). Thus, the method taught by Wolff would anticipate delivering a heterologous nucleic acid to a human with AAV-2 antibodies since the vast majority of humans would be expected to be AAV-2 seropositive.

Claims 1, 2, 6, 7, 13, 14, 16-20, and 27-28 are rejected under 35 U.S.C. 102(e) as being anticipated by Chiorini et al., (US 2003/0215422) as evident by Couto et al. (US Patent 6,200,560).

Chiorini teaches a method of delivering AAV to a cell of the submandibular gland derived from a human, wherein the AAV comprises a heterologous nucleic acid encoding human Factor IX, wherein human Factor IX is expressed at a therapeutic level (pages 3 and 9). Administering the rAAV to the bile duct of the submandibular gland of a human would result in the Factor IX being secreted into an extracellular space and blood vessels of the human.

Couto teaches that 85% of the human population is seropositive for AAV-2 serotype (column 12). Thus, the method taught by Chiorini would anticipate delivering Factor IX to a human with AAV-2 antibodies since the vast majority of humans would be expected to be AAV-2 seropositive.

Claims 1, 2, 6, 7, 13, 14, 16-20, and 27-28 are rejected under 35 U.S.C. 102(e) as being anticipated by McClelland et al., (US 2003/0147853) as evident by Couto et al. (US Patent 6,200,560).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

McClelland teaches a method of delivering rAAV virions comprising a heterologous gene encoding human Factor IX to a duct of the liver of the submandibular gland of a human (pages 2, 6, and 9-11). McClelland also teaches using the method to treat hemophilia in a human (pages 6 and 9-11). Administering the rAAV to the bile duct of the liver of a human would result in the Factor IX being secreted into an extracellular space and blood vessels of the human.

Couto teaches that 85% of the human population is seropositive for AAV-2 serotype (column 12). Thus, the method taught by McClelland would anticipate delivering Factor IX to a human with AAV-2 antibodies since the vast majority of humans would be expected to be AAV-2 seropositive.

Claims 1, 2, 6, 7, 13, 14, 16-20 and 27-28 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. US application 10/100,235 (pre-grant US publication 2003/0147853) claims a method of delivering rAAV virions comprising a

heterologous gene encoding human Factor IX to a duct of the liver of the submandibular gland of a human. US application '235 also claims using the claimed method to treat hemophilia in a human.

Couto teaches that 85% of the human population is seropositive for AAV-2 serotype (column 12). Thus, the method claimed by McClelland would anticipate delivering Factor IX to a human with AAV-2 antibodies since the vast majority of humans would be expected to be AAV-2 seropositive.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 2, 6, 7, 13, 14, 16-20 and 27-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Snyder et al., (US 2002/0151509) taken with Yang et al., (PNAS, 90:4601-4605, 1993).

Snyder teaches a gene therapy method of treating hemophilia in a mammal, preferably a human, comprising administering a recombinant adeno-associated vector comprising a promoter operatively linked to a polynucleotide encoding human blood coagulation protein to a duct of the liver in the mammal (pages 2, 3, 4, 5, 7, 9 and 15-17). The blood coagulation protein can be Factor IX for treating hemophilia B (pages 6 and 7). Administering the rAAV to the bile duct of the liver of a human would result in the Factor IX being secreted into an extracellular space and blood vessels of the human. However, Snyder does not specifically teach administering to the bile duct system of a human.

However, at the time the invention was made, Yang teaches that retrograde administration of a viral vector into the biliary tract through the common bile duct results in gene expression in all cells of the intra-hepatic bile duct in vivo (pages 4601 and 4603).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching Snyder taken with Yang to administer AAV to the common bile duct in a gene therapy method for treating hemophilia in a mammal. One of ordinary skill in the art would have been motivated to administer AAV to the bile duct system using retrograde administration because Yang teaches that this route of administration results in heterologous gene expression in virtually all cells of the intra-hepatic duct in vivo.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 6, 7, 13, 14, 16-20, and 27-28 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-36 of copending Application No. 10/100,235 in view of Couto et al. (US Patent 6,200,560). '235 claims a method of delivering rAAV virions comprising a heterologous gene encoding human Factor IX to a duct of the liver or the submandibular gland of a human. '235 also claims using the claimed method to treat hemophilia in a human. However, '235 does not specifically teach wherein said human has pre-existing anti-AAV antibodies.

However, Couto teaches that 85% of the human population is seropositive for AAV-2 serotype (column 12). Thus, the method claimed by McClelland would read on delivering Factor IX to a human with AAV-2 antibodies since the vast majority of humans would be expected to be AAV-2 seropositive.

This is a provisional obviousness-type double patenting rejection.

Claims 1, 2, 6, 7, 13, 14, 16-20 and 27-28 are directed to an invention not patentably distinct from claims 1-36 of commonly assigned US application 10/100,235 as evident by Couto et al. (US Patent 6,200,560).

Specifically, '235 claims a method of delivering rAAV virions comprising a heterologous gene encoding human Factor IX to a duct of the liver of the submandibular gland of a human. '235 also claims using the claimed method to treat hemophilia in a human. However, '235 does not specifically teach wherein said human has pre-existing anti-AAV antibodies.

However, Couto teaches that 85% of the human population is seropositive for AAV-2 serotype (column 12). Thus, the method claimed by McClelland would read on delivering Factor IX to a human with AAV-2 antibodies since the vast majority of humans would be expected to be AAV-2 seropositive.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned application, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Conclusion

If a copy of a provisional application listed on the bottom portion of the accompanying Notice of References Cited (PTO-892) form is not included with this Office action and the PTO-892 has been annotated to indicate that the copy was not readily available, it is because the copy could not be readily obtained when the Office action was mailed. Should applicant desire a copy of such a provisional application, applicant should promptly request the copy from the Office of Public Records (OPR) in accordance with 37 CFR 1.14(a)(1)(iv), paying the required fee under 37 CFR 1.19(b)(1). If a copy is ordered from OPR, the shortened statutory period for reply to this Office action will not be reset under MPEP § 710.06 unless applicant can demonstrate a substantial delay by the Office in fulfilling the order for the copy of the provisional application. Where the applicant has been notified on the PTO-892 that a copy of the provisional application is not readily available, the provision of MPEP § 707.05(a) that a copy of the cited reference will be automatically furnished without charge does not apply.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, SPE - Art Unit 1635, can be reached at (571) 272-0760.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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